

Figure 1a

1 MALPNKEFLW FCCFAWLCFP ISLDLPSRG EAQIVARTAL ESEAETWSLL

R87H [E1]

▽

51 NHLGGRHRPG LLSPILLEVLY DGHGEPPRLQ PDDRALRYMK RLYKAYATKE

101 GTPKSNRRHL YNTVRLFTPQ AQHQQAPGDL AAGTFPSVDL LFNLDRTVW

151 EHLFKSVLLY TFNNISFPPF PVKCICNLVI KEPEFSSKTL PRAPYSFTYN

E241K [324]

▽

201 SQFEFRKKYK WMEIDVTAPL EPLVASHKRN IHMSVNFTCA EDQLQHPSAR

251 DSLFNMTLLV APSLLYLND TSAQAFHRWH SLHPKRKPSQ GPDQKRGGLSA

(1)

V332I [597]

301 YPVGEEAAEG VRSS█████RDQ ESASSELKKP LVPASVNLSE YFKQFLFPQN

V371M [714]

S395F [787]

▽

351 ECELHDFRLS FSQLKWDNWI VAPHKYNPRY CKGDCPRAVG HRYG██PVHTM

401 VQNIIHEKLD SSVPRPSCVP AKYSPLSVLA IEPDGSIAYK EYEDMIATKC

(135)

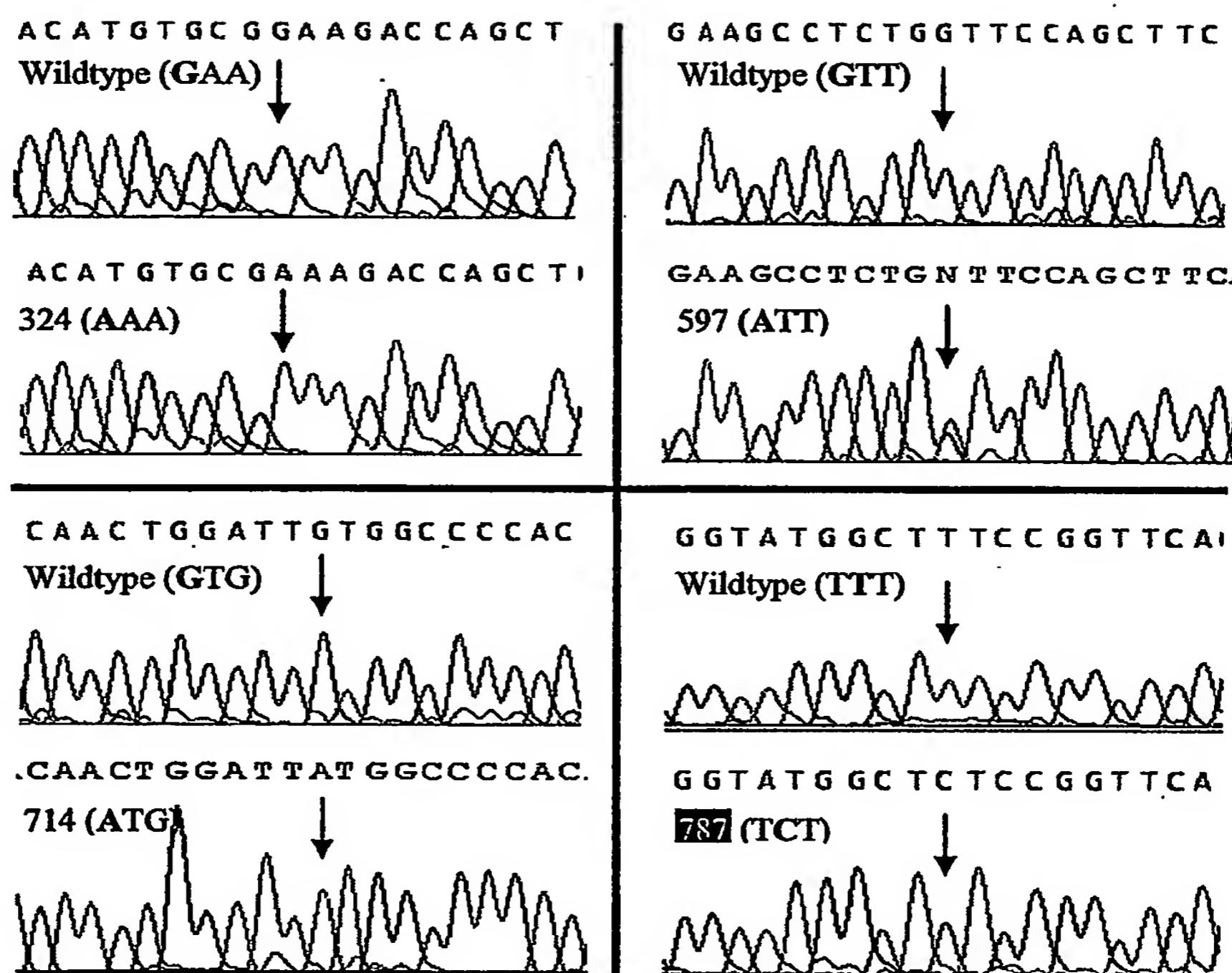
Figure 1b

Figure 2a

1 MVLLSILRIL ▽ LWGLVLFM EH RVQMTQVGQP SIAHLPEAPT LPLIQELLEE
51 APGKQQRKPR VLGHPLRYML ELYQRSADAS GHPRENRTIG ATMVRLVRPL
101 ASVARPLRGS WHIQTLD FPL RPNRVAYQLV RATVVYRHQL HLTHSHLSCH
151 VEPWVQKSPT NHFPSSGRGS SKPSLLPKTW TEMDIMEHVG QKLWNHKGRR

Q239Ter [S1]

201 VLRLRFVCQQ PRGSEVLEFW WHGTSSLD TV FLLLYFNDT Q SVQKTKPLPK
(1)
251 GLKEFTEKDP SLLI [REDACTED] Q GSIASEVPGP SREHDGPESN QCSLHPFQVS
301 FQQLGWDHWI IAPHLYTPNY CKGVCPRVLH YGLNSPNHAI IQNLVSELVD

S367I [S2]

(125)

351 QNVPQPSCVP YKYVPI SILL IEANGSILYK EYEGMIAQSC TCR

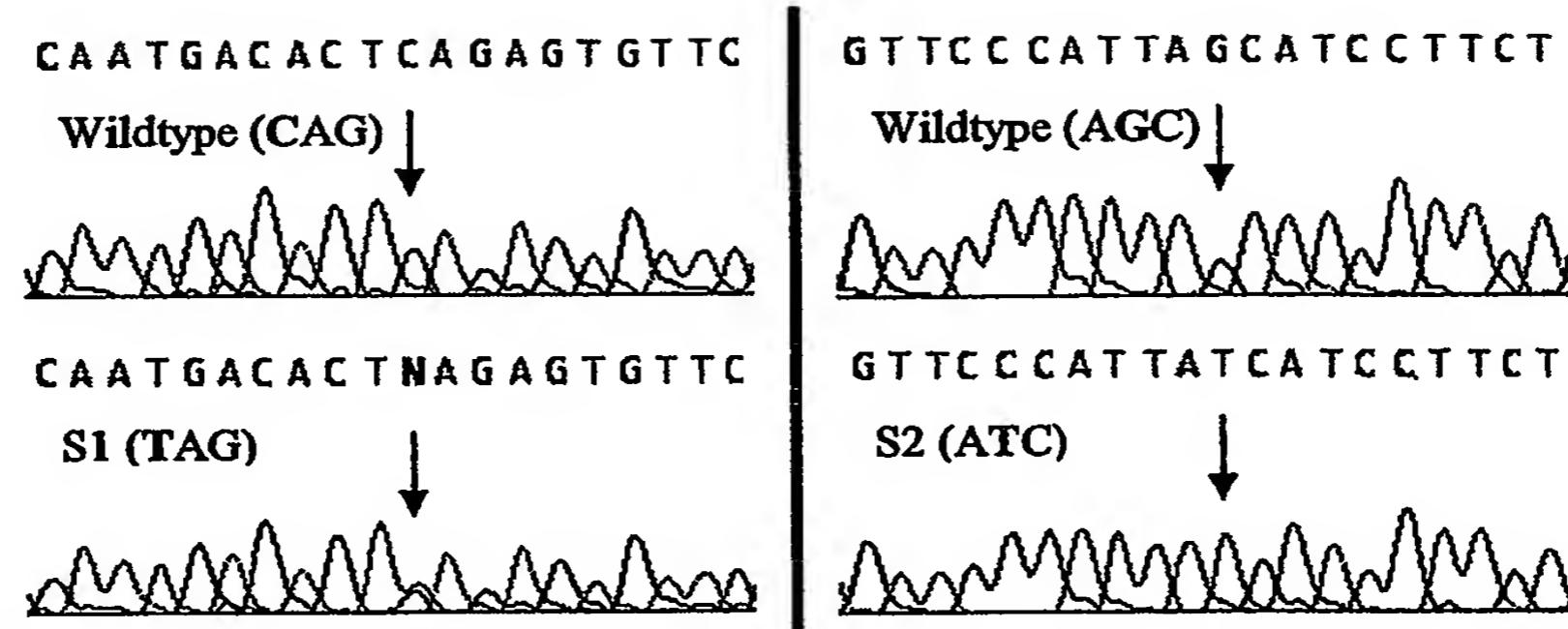
Figure 2b

Figure 3a

Animal	R	9 3 0 3 0	9 3 0 4 5	9 7 0 4 5	9 0 8 8 1	9 0 8 8 1	8 7 8 8 3	9 0 8 8 1	9 4 8 3 0	7 8 1 0
Phenotype	n/a	S	S	F	S	S	F	F	F	F
GENOTYPE	S1	+/Y	S1/+	S1/+	S1/+	+/+	+/+	+/+	+/+	+/+
	S2	S2/Y	S2/+	S2/+	+/+	S2/+	S2/+	+/+	S2/+	S2/+
	787	T/+	T/+	+/+	+/+	T/T	T/T	T/+	+/+	+/+

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Figure 3b

Animal		9 6 2 1 0 1	9 9 7 6 3 4	9 9 7 6 3 5	9 9 7 1 5 2	9 9 7 5 5 3	9 7 6 2 3 4	9 3 0 1 4 2	9 4 8 0 9 3	8 8 7 7 4	
Phenotype											
Sterile (S)	n/a	S	S	F	F	S	F	n/a	S	F	
Fertile (F)											
G E N O T Y P E	S1	S1/Y	S1/S1	S1/S1	S1/+	S1/+	S1/S1	S1/+	S1/Y	S1/+	+/+
	S2	+/Y	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+	+/+
	787	T/+	T/T	T/T	T/+	T/+	T/+	+/+	T/T	T/T	T/+

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Figure 4**Sheep GDF9**

atg	gcg	ctt	ccc	aac	aaa	ttc	ttc	ctt	tgg	ttt	tgc	tgc	ttt	gcc	45	
Met	Ala	Leu	Pro	Asn	Lys	Phe	Phe	Leu	Trp	Phe	Cys	Cys	Phe	Ala		
-315								-310					-305			
tgg	ctc	tgt	ttt	cct	att	agc	ctt	gat	tct	ctg	cct	tct	agg	gga	90	
Trp	Leu	Cys	Phe	Pro	Ile	Ser	Leu	Asp	Ser	Leu	Pro	Ser	Arg	Gly		
-300								-295					-290			
gaa	gct	cag	att	gta	gct	agg	act	gcg	ttg	gaa	tct	gag	gct	gag	135	
Glu	Ala	Gln	Ile	Val	Ala	Arg	Thr	Ala	Leu	Glu	Ser	Glu	Ala	Glu		
-285								-280					-275			
act	tgg	tcc	ttg	ctg	aac	cat	tta	ggt	ggg	aga	cac	aga	cct	ggt	180	
Thr	Trp	Ser	Leu	Leu	Asn	His	Leu	Gly	Gly	Arg	His	Arg	Pro	Gly		
-270								-265					-260			
ctc	ctt	tcc	cct	ctc	tta	gag	gtt	ctg	tat	gat	ggg	cac	ggg	gaa	225	
Leu	Leu	Ser	Pro	Leu	Leu	Glu	Val	Leu	Tyr	Asp	Gly	His	Gly	Glu		
-255								-250					-245			
[E1]																
ccc	ccc	agg	ctg	cag	cca	gat	gac	aga	gct	ttg	cgc	tac	atg	aag	270	
Pro	Pro	Arg	Leu	Gln	Pro	Asp	Asp	Arg	Ala	Leu	<u>Arg</u>	Tyr	Met	Lys		
-240								-235					-230			
agg	ctc	tat	aag	gca	tac	gct	acc	aag	gag	ggg	acc	cct	aaa	tcc	315	
Arg	Leu	Tyr	Lys	Ala	Tyr	Ala	Thr	Lys	Glu	Gly	Thr	Pro	Lys	Ser		
-225								-220					-215			
aac	aga	cgc	cac	ctc	tac	aac	act	gtt	cgg	ctc	ttc	acc	ccc	tgt	360	
Asn	Arg	Arg	His	Leu	Tyr	Asn	Thr	Val	Arg	Leu	Phe	Thr	Pro	Cys		
-210								-205					-200			
Intron position																
gct	cag	cac	aag	cag	gct	cct	ggg	gac	ctg	gcg	gca	g	ga	acc	ttt	405
Ala	Gln	His	Lys	Gln	Ala	Pro	Gly	Asp	Leu	Ala	Ala	<u>Gly</u>	Thr	Phe		
-195								-190					-185			
cca	tca	gtg	gat	ctg	ctg	ttt	aac	ctg	gat	cgt	gtt	act	gtt	gtg	450	
Pro	Ser	Val	Asp	Leu	Leu	Phe	Asn	Leu	Asp	Arg	Val	Thr	Val	Val		
-180								-175					-170			
[74] [80]																
gaa	cat	tta	ttc	aag	tca	gtc	ttg	ctg	tat	act	ttc	aac	aac	tcc	495	
Glu	His	Leu	Phe	Lys	Ser	Val	Leu	Leu	Tyr	Thr	Phe	Asn	Asn	Ser		
-165								-160					-155			
att	tct	ttt	ccc	ttt	cct	gtt	aaa	tgt	ata	tgc	aac	ctg	gtg	ata	540	
Ile	Ser	Phe	Pro	Phe	Pro	Val	Lys	Cys	Ile	Cys	Asn	Leu	Val	Ile		
-150								-145					-140			
aaa	gag	cca	gag	ttt	tct	agc	aag	act	ctc	cct	aga	gct	cca	tac	585	
Lys	Glu	Pro	Glu	Phe	Ser	Ser	Lys	Thr	Leu	Pro	Arg	Ala	Pro	Tyr		
-135								-130					-125			
tca	ttt	acc	tat	aac	tca	cag	ttt	gaa	ttt	aga	aag	aaa	tac	aaa	630	
Ser	Phe	Thr	Tyr	Asn	Ser	Gln	Phe	Glu	Phe	Arg	Lys	Lys	Tyr	Lys		
-120								-115					-110			
tgg	atg	gag	att	gat	gtg	acg	gct	cct	ctt	gag	cct	ctg	gtg	gcc	678	
Trp	Met	Glu	Ile	Asp	Val	Thr	Ala	Pro	Leu	Glu	Pro	Leu	Val	Ala		
-105								-100					-95			
[324]																

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Figure 4 continued

cac aag agg aat att cac atg tct gta aat ttt aca tgt gcg gaa gac His Lys Arg Asn Ile His Met Ser Val Asn Phe Thr Cys Ala <u>Glu</u> Asp -90 -85 -80	726
cag ctg cag cat cct tca gcg cg ^g gac agc ctg ttt aac atg act ctt Gln Leu Gln His Pro Ser Ala Arg Asp Ser Leu Phe Asn Met Thr Leu -75 -70 -65	774
ctc gta gcg ccc tca ctg ctt ttg tat ctg aac gac aca agt gct cag Leu Val Ala Pro Ser Leu Leu Tyr Leu Asn Asp Thr Ser Ala Gln -60 -55 -50 -45	822
gct ttt cac agg tgg cat tcc ctc cac cct aaa agg aag cct tca cag Ala Phe His Arg Trp His Ser Leu His Pro Lys Arg Lys Pro Ser Gln -40 -35 -30	870
ggt cct gac cag aag aga ggg cta tct gcc tac ccc gtg gga gaa gaa Gly Pro Asp Gln Lys Arg Gly Leu Ser Ala Tyr Pro Val Gly Glu Glu -25 -20 -15	918
gct gct gag ggt gta aga tcg tcc cgt cac cgc aga gac cag gag agt Ala Ala Glu Gly Val Arg Ser Ser Arg His Arg Arg Asp Gln Glu Ser -10 -5 -1 1	966
[581] [597] gcc agc tct gaa ttg aag aag cct ctg gtt cca gct tca gtc aat ctg Ala Ser Ser Glu Leu Lys Lys Pro Leu <u>Val</u> Pro Ala Ser Val Asn Leu 5 10 15 20	1014
agt gaa tac ttc aaa cag ttt ctt ttt ccc cag aat gaa tgt gag ctc Ser Glu Tyr Phe Lys Gln Phe Leu Phe Pro Gln Asn Glu Cys Glu Leu 25 30 35	1062
cat gac ttt aga ctt agc ttt agt cag ctg aag tgg gac aac tgg att His Asp Phe Arg Leu Ser Phe Ser Gln Leu Lys Trp Asp Asn Trp Ile 40 45 50	1110
[714] gtg gcc cca cac aaa tac aac cct cga tac tgt aaa ggg gac tgt ccc Val Ala Pro His Lys Tyr Asn Pro Arg Tyr Cys Lys Gly Asp Cys Pro 55 60 65	1158
[787] agg gcg gtc gga cat cgg tat ggc tct ccg gtt cac acc atg gtg cag Arg Ala Val Gly His Arg Tyr Gly <u>Ser</u> Pro Val His Thr Met Val Gln 70 75 80	1206
aac atc atc cat gag aaa ctt gac tcc tca gtg cca aga cca tcc tgt Asn Ile Ile His Glu Lys Leu Asp Ser Ser Val Pro Arg Pro Ser Cys 85 90 95 100	1254
gta cct gcc aag tat agc cct ttg agt gtt ttg gcc atc gag cct gat Val Pro Ala Lys Tyr Ser Pro Leu Ser Val Leu Ala Ile Glu Pro Asp 105 110 115	1302
ggc tca atc gct tat aaa gaa tat gaa gat atg ata gcc act aag tgt Gly Ser Ile Ala Tyr Lys Glu Tyr Glu Asp Met Ile Ala Thr Lys Cys 120 125 130	1350
acc tgt cgt taa cagactc ctgtcaagta aaaccatgag tgtcctggcc Thr Cys Arg STOP 135	1399
agtgtaaatg ccgcgc 1416	

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Figure 5

Sheep BMP15 full

aca cag gta ggg cag ccc tct att gcc cac ctg cct gag gcc cct 117
 Thr Gln Val Gly Gln Pro Ser Ile Ala His Leu Pro Glu Ala Pro
 -240 -235 -230

acc ttg ccc ctg att cag gag ctg cta gaa gaa gcc cct ggc aag 162
 Thr Leu Pro Leu Ile Gln Glu Leu Leu Glu Glu Ala Pro Gly Lys
 -225 -220 -215

cag cag agg aag ccg cggttc tta ggg cat ccc tta cggtat atg 207
 Gln Gln Arg Lys Pro Arg Val Leu Gly His Pro Leu Arg Tyr Met
 -210 -205 -200

ctg gag ctg tac cag cgt tca gct gac gca agt gga cac cct agg 252
 Leu Glu Leu Tyr Gln Arg Ser Ala Asp Ala Ser Gly His Pro Arg
 -195 -190 -185

gaa aac cgc acc att ggg gcc acc atg gtg agg ctg gtg agg ccg 297
 Glu Asn Arg Thr Ile Gly Ala Thr Met Val Arg Leu Val Arg Pro
 -180 -175 -170

tcc tgg cac ata cag acc ctg gac ttt cct ctg aga cca aac cgg 372
 Ser Trp His Ile Gln Thr Leu Asp Phe Pro Leu Arg Pro Asn Arg
 . -155 -150 -145

gta gca tac caa cta gtc aga gcc act gtg gtt tac cgc cat cag 417
 Val Ala Tyr Gln Leu Val Arg Ala Thr Val Val Tyr Arg His Gln
 -140 -135 -130

ctt cac cta act cat tcc cac ctc tcc tgc cat gtg gag ccc tgg 462
 Leu His Leu Thr His Ser His Leu Ser Cys His Val Glu Pro Trp
 -125 -120 -115

gtc cag aaa agc cca acc aat cac ttt cct tct tca gga aga ggc 507
 Val Gln Lys Ser Pro Thr Asn His Phe Pro Ser Ser Gly Arg Gly
 -110 -105 -100

atg gaa cat gtt ggg caa aag ctc tgg aat cac aag ggg cgc agg gtt 603
 Met Glu His Val Gly Gln Lys Leu Trp Asn His Lys Gly Arg Arg Val
 -80 -75 -70

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Figure 5 continued

cta cga ctc cgc ttc gtg tgt cag cag cca aga ggt agt gag gtt ctt	651
Leu Arg Leu Arg Phe Val Cys Gln Gln Pro Arg Gly Ser Glu Val Leu	
-65 -60 -55	
gag ttc tgg tgg cat ggc act tca tca ttg gac act gtc ttc ttg tta	699
Glu Phe Trp Trp His Gly Thr Ser Ser Leu Asp Thr Val Phe Leu Leu	
-50 -45 -40	
[S1]	[422]
ctg tat ttc aat gac act <u>G</u> ag agt gtt cag aag acc aaa cct ctc cct	747
Leu Tyr Phe Asn Asp Thr <u>Gln</u> Ser Val Gln Lys Thr Lys Pro Leu Pro	
-35 -30 -25 -20	
aaa ggc ctg aaa gag ttt aca gaa aaa gac cct tct ctt ctc ttg agg	795
Lys Gly Leu Lys Glu Phe Thr Glu Lys Asp Pro Ser Leu Leu Leu Arg	
-15 -10 -5	
agg gct cgt caa gca ggc agt att gca tcg gaa gtt cct ggc ccc tcc	843
Arg Ala Arg Gln Ala Gly Ser Ile Ala Ser Glu Val Pro Gly Pro Ser	
-1 1 ' 5 10	
agg gag cat gat ggg cct gaa agt aac cag tgt tcc ctc cac cct ttt	891
Arg Glu His Asp Gly Pro Glu Ser Asn Gln Cys Ser Leu His Pro Phe	
15 20 *** 25	
caa gtc agc ttc cag cag ctg ggc tgg gat cac tgg atc att gct ccc	939
Gln Val Ser Phe Gln Gln Leu Gly Trp Asp His Trp Ile Ile Ala Pro	
30 *** 35 40 45	
cat ctc tat acc cca aac tac tgt aag gga gta tgt cct cgg gta cta	987
His Leu Tyr Thr Pro Asn Tyr Cys Lys Gly Val Cys Pro Arg Val Leu	
50 . 55 60	
cac tat ggt ctc aat tct ccc aat cat gcc atc atc cag aac ctt gtc	1035
His Tyr Gly Leu Asn Ser Pro Asn His Ala Ile Ile Gln Asn Leu Val	
65 70 . 75	
agt gag ctg gtg gat cag aat gtc cct cag cct tcc tgt gtc cct tat	1083
Ser Glu Leu Val Asp Gln Asn Val Pro Gln Pro Ser Cys Val Pro Tyr	
80 85 90	
[S2]	
aag tat gtt ccc att <u>agc</u> atc ctt ctg att gag gca aat ggg agt atc	1131
Lys Tyr Val Pro Ile <u>Ser</u> Ile Leu Leu Ile Glu Ala Asn Gly Ser Ile	
95 100 105	
ttg tac aag gag tat gag ggt atg att gcc cag tcc tgc aca tgc agg	1179
Leu Tyr Lys Glu Tyr Glu Gly Met Ile Ala Gln Ser Cys Thr Cys Arg	
110 115 120 125	
tga cggcaaagggtgca	
STOP	

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Figure 6

BMP2 Human
 BMP7/OP1 Human
 GDF9 SHEEP
 GDF9 Human
 GDF9 Mouse
 GDF9B SHEEP
 GDF9B Mouse
 GDF9B Human
 TGFB2 Human
 TGFB3 Human
 TGFB1 Human

[REDACTED] QAKHKQRKRLKS-----S[KR]HPLYVDES-DVGWND
 [REDACTED] STGSKQRSQNRSKTPKNQEALRMANVAENSSDQRQA[KK]HELYVSFR-DLGWQD
 [REDACTED] RRRDQESASSELKKPLVPASVNLSEYFKQFLFP----QNE[GEL]HDFRLSFS-QLKWDN
 [REDACTED] RRR[GQETVSSELKKPLGPASFNLSEYFRQFLP----QNE[GEL]HDFRLSFS-QLKWDN
 [REDACTED] RRAQAGSIASEVPGPSREHDGPE-----SNQ[SL]HPFQVSEQ-QLGWDH
 [REDACTED] QACSI[SDASCPSQEHGSV-----NNQ[SL]HPYKVSEH-QLGWDH
 [REDACTED] QADGISAEVTA[SSK]HSGPE-----NNQ[SL]HPFQISFR-QLGWDH
 [REDACTED] ALDAAYCFRNQDN-----CLRPLYIDEKRDLGWK-
 [REDACTED] ALDTNYCFRNLEEN-----CVRPLYIDEFRQDLGWK-
 [REDACTED] ALDTNYCFSSTEKN-----CVRQLYIDEFRKDLGWK-

0 10 20 30 40 50

BMP2 Human
 BMP7/OP1 Human
 GDF9 SHEEP
 GDF9 Human
 GDF9 Mouse
 GDF9B SHEEP
 GDF9B Mouse
 GDF9B Human
 TGFB2 Human
 TGFB3 Human
 TGFB1 Human

WIVAPPGYHAFY[HGE]PFPLADHLNSTNHAIVQTLVNSVN-SKI PKA[VPTELSAISM
 WIIAPEGYAAYY[EGE]AFPLNSYMNATNHAIVQTLVHFINPETVPKPEAPTQLNAISV
 WIVAPHKYNPRY[KGD]PRAVGHRYG[SP]VHTMVQNI[IHEKLDSSVPRPS]VPAKYSPLSV
 WIVAPHRYNPRY[KGD]PRAVGHRYGSPVHTMVQNI[IYEKLDSSVPRPS]VPAKYSPLSV
 WIVAPHRYNPRY[KGD]PRAVRHRYGSPVHTMVQNI[IYEKLDPSVPRPS]VPGKYSPLSV
 WIIAPHLYT[PNY]KG[V]PRVLHYGLNSPNHAI[IONL]VSELVDQNPQPS[VPYKYVPI]SI
 WIIAPRLYT[PNY]KG[V]TRVLPYGLNSPNHAI[IONL]VSELVDQNPQPS[VPYNFLPMSI
 WIIAPPFYTPNY[KGT]LRVLRDGLNSPNHAI[IONL]INQLVDQSVPRPS[VPYKYVPI]SV
 WIHEPKGYNANF[AGA]SPYLWS---SDTQHSRVLSLYNTINPEASASP[VSDLEPLTI
 WVHEPKGYYANF[SGP]SPYLRS---ADTT[HSTV]LGLYNTLNPEASASP[VSDLEPLTI
 WIHEPKGYHANF[SLGP]SPYIWS---LDTQYSKVLALYNQHNP[GASAAP]VPQALEPLPI

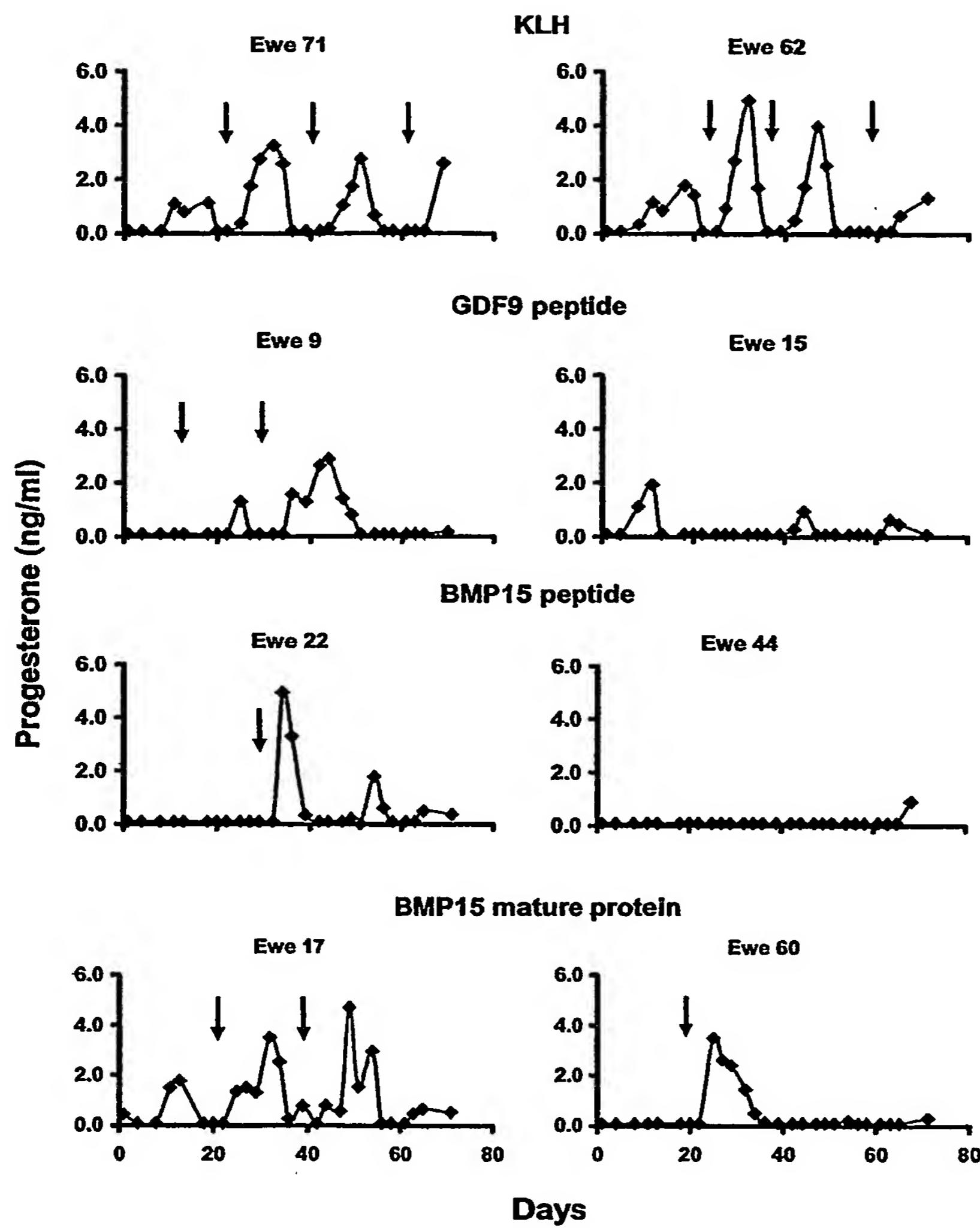
60 70 80 90 100 * 110

BMP2 Human
 BMP7/OP1 Human
 GDF9 SHEEP
 GDF9 Human
 GDF9 Mouse
 GDF9B SHEEP
 GDF9B Mouse
 GDF9B Human
 TGFB2 Human
 TGFB3 Human
 TGFB1 Human

LYLDENEKVVLKNYQDMVVEG[G]R
 LYFDDSSNVILKKYRNMVVRA[G]H
 LAIEPDGSIAYKEYEDMIATKET[R]
 LTIEPDGSIAYKEYEDMIATKET[R]
 LTIEPDGSIAYKEYEDMIATR[R]
 LLIEANGSILYKEYEGMIAQSET[R]
 LLIETNGSILYKEYEGMIAQSET[R]
 LMIEANGSILYKEYEGMIAES[R]
 LYYIGK-TPKIEQLSNMIVKS[K]S
 LYYVGR-TPKVEQLSNMVVK[S]K
 VYYVGR-KPKVEQLSNMIVRS[K]S

120 130 140

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Figure 7

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Figure 8